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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
STEADMAN, DAVID J	
ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 04/09/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/407,806	MURPHY ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1652	

-- The MAILING DATE of this communicati n appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,13,14 and 17-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,13,14 and 17-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Application Status

Claims 1-9, 13, 14, and 17-23 are pending in the application.

The finality of the rejection of the Office action of Paper No. 13 is withdrawn and prosecution has been reopened.

Applicants' amendment to claims 14 and 17-19 and cancellation of claims 10-12 in Paper No. 14 is acknowledged.

Applicants' arguments presented in Paper No. 14 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Specification/Informalities

1. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: "*Thermococcus alcaliphilus* Alpha-Galactosidase". See MPEP § 606.01.

Claim Rejections - 35 USC § 112, Second Paragraph

2. Claims 1-9, 13, 14, and 17-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. Claims 1 (claims 2-4, 6-9, 13, 14, and 17-23 dependent therefrom) and 5 are indefinite in the recitation of "a polynucleotide that is complementary". Neither the specification nor the claims provides a definition of the term "complementary" and it is unclear whether the complementary strand(s) is a partial or complete complement. It is suggested that Applicants clarify their meaning of the term "a

polynucleotide that is complementary" with, for example, "a polynucleotide that is completely complementary".

4. Claim 9 is unclear in the recitation of "process of producing a cell". It is unclear as to how the recited steps result in the production of a cell. It is suggested that the term "process of producing a cell" be replaced with, for example, "process of transforming or transfecting a cell".

Claim 13 (claims 14 and 19 dependent therefrom) is unclear in the recitation of "protein having enzymatic activity". It is unclear as to whether applicants intend for the encoded protein to have alpha-galactosidase enzymatic activity as the claims and specification would suggest or some other enzymatic activity. It is suggested that applicants clarify the meaning of the claim. The examiner has interpreted the claim as a protein having alpha-galactosidase enzymatic activity. If the Examiner's interpretation of these claims is incorrect, Applicant should so state and clarify the record.

Claim Rejections - 35 USC § 112, First Paragraph

5. Claims 1-3, 5-9, and 17-23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1 (claims 2, 3, 6-9, 17-23 dependent therefrom) and 5 (claims dependent therefrom) are directed to a genus of polynucleotides having at least 70 % identity to a polynucleotide encoding an alpha-galactosidase comprising SEQ ID NO:4 (part (a) of claim 1) or a genus of polynucleotides comprising at least 30 nucleotides thereof (part (c) of claim 1) and a genus of polynucleotides having at least 90 % identity to a polynucleotide encoding an alpha-galactosidase comprising SEQ ID NO:4 (part (a) of claim 5) or a genus of polynucleotides comprising at least 30 nucleotides thereof (part (c) of claim 5). The specification does not contain any disclosure of the function of all polynucleotides comprising homologues or fragments of a polynucleotide encoding SEQ ID NO:4 as encompassed by the claims. The genus of claimed polynucleotides is a large variable genus with the potentiality of encoding many

different proteins. Therefore, many functionally unrelated polynucleotides are encompassed within the scope of these claims, including partial polynucleotide sequences. The specification discloses only a single species of the claimed genus, i.e., SEQ ID NO:3, which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicants argue that claim 19 depends from claim 1 which recites polynucleotides encoding enzymes having alpha-galactosidase enzymatic activity and therefore, the polynucleotide of claim 19 would be so limited in scope to incorporate this limitation. Applicants argue that the amendment to replace "an enzyme" with "an alpha galactosidase" further limits the genus of claimed polynucleotides to those encoding alpha galactosidase enzymes. Applicants' argument is not found persuasive. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. The claimed genus of polynucleotides, while limited by structure to a polynucleotide having at least 70 % or 90 % identity to a polynucleotide encoding SEQ ID NO:4 or a polynucleotide comprising at least 30 bases thereof, are not limited to polynucleotides encoding polypeptides with alpha galactosidase activity. As written, the claimed genus of polynucleotides can encode polypeptides with or without any enzymatic activity. As such, applicants have failed to sufficiently describe the claimed genus of polynucleotides such that one skilled in the art can reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

6. Claims 1-3, 5-9, and 17-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polynucleotide of SEQ ID NO:3, does not reasonably provide enablement for *all* polynucleotides having at least 70 % identity to a polynucleotide encoding an alpha-

galactosidase comprising SEQ ID NO:4 (part (a) of claim 1), *all* polynucleotides comprising at least 30 nucleotides thereof (part (c) of claim 1), *all* polynucleotides having at least 90 % identity to a polynucleotide encoding an alpha-galactosidase comprising SEQ ID NO:4 (part (a) of claim 5) or *all* polynucleotides comprising at least 30 nucleotides thereof (part (c) of claim 5). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re* Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1 (claims 2, 3, 6-9, 17-23 dependent therefrom), 5 (claims dependent therefrom), 13, and 14 are so broad as to encompass *all* polynucleotides comprising homologues or fragments of a polynucleotide encoding SEQ ID NO:4 as encompassed by the claims. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claims. Since the nucleic acid sequence of a encoding polynucleotide determines a polypeptide's structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the polynucleotide of SEQ ID NO:3.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple nucleotide substitutions or modifications, as encompassed by the instant claims, and the positions within an encoded protein's sequence where amino acid modifications can be made with a

reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass polynucleotide homologues or fragments of a polynucleotide encoding SEQ ID NO:4 encoding polyeptides with or without all enzymatic activities because the specification does not establish: (A) regions of the polynucleotide structure which may be modified without affecting alpha-galactosidase activity; (B) the general tolerance of the alpha-galactosidase of SEQ ID NO:4 to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any nucleotides of SEQ ID NO:3 or a polynucleotide encoding SEQ ID NO:4 with an expectation of encoding a polypeptide with the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of amino acid modifications of *all* polynucleotides comprising homologues or fragments of a polynucleotide encoding SEQ ID NO:4 as encompassed by the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re* Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re* Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Conclusion

7. All claims are rejected.

8. No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The Examiner can normally be reached Monday-Friday from 7:30 am to 2:00 pm and from 3:30 pm to 5:30 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX number for this Group is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman, Ph.D.

REBECCA E. PROUTY
PRIMARY EXAMINER
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